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NOTICE OF ALLOWANCE AND FEE(S) DUE

26710 7590 07/31/2008

QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE
SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 07/31/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,870	07/23/2003	Howard J. Jacob	650053.00002	8005

TITLE OF INVENTION: RAT MODEL OF DIABETIC NEPHROPATHY

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1440	$300	$0	$1740	10/31/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,870	07/23/2003	Howard J. Jacob	650053.00002	8005

TITLE OF INVENTION: RAT MODEL OF DIABETIC NEPHROPATHY

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1440	$300	$0	$1740	10/31/2008

EXAMINER	ART UNIT	CLASS-SUBCLASS
POPA, ILEANA	1633	800-009000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☐ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 103 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 103 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/625,870	JACOB ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *02/25/2008*.

2. ☒ The allowed claim(s) is/are *1,3,4 and 6-12*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

Election/Restrictions

1. Claims 11 and 12 are allowable. The restriction requirement between the inventions of Groups I (claims 1-10) and II (claims 11 and 12), as set forth in the Office action mailed on 11/16/2005, has been reconsidered in view of the allowability of claims to the elected invention pursuant to MPEP § 821.04(a). **The restriction requirement between the inventions of Groups I and II is hereby withdrawn as to any claim that requires all the limitations of an allowable claim.** In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 13-17, directed to methods of evaluating the effect of a test compound on cardiac, vascular, or eye damage stand withdrawn from further consideration because do not require all the limitations of an allowable generic linking claim as required by 37 CFR 1.141.

2. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided

by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview with Jean Baker on 7/10/2008.

The application has been amended as follows:

Claims 3, 5, and 13-17 are cancelled.

Claim 1 is rewritten as follows:

--**"A rat diabetes model, wherein the rat develops symptoms of type II diabetes and progressive diabetic nephropathy with nodule formation and wherein the rat is a T2DN rat comprising mitochondrial genome at loci on chromosomes 2 (D2Rat12), 11 (D11Rat93), 16 (D16Rat15), 19 (D19Rat59), and X (DXMit4 and DXMit42) from a Fawn Hooded rat into a GK rat, wherein the T2DN rat does not comprise GK alleles at markers D3Rat57, D11Mgh5, D12Rat22, D1Rat 291, D1Mit18, D1Mit34, D1Mgh12, and D1Rat85, and wherein the T2DN rat develops progressive proteinuria and glomerulosclerosis leading to diabetic nephropathy."**

Claim 4 is rewritten as follows:

--**"The T2DN rat of claim 1 wherein the T2DN rat is further genetically altered by introducing additional genetic material.**

Claim 6 is rewritten as follows:

--**"The T2DN rat of claim 1 wherein the T2DN rat is further genetically altered by introducing genetic deletions."**

Claim 7 is rewritten as follows:

--**"A rat comprising mitochondrial genome at loci on chromosomes 2 (D2Rat12), 11 (D11Rat93), 16 (D16Rat15), 19 (D19Rat59), and X (DXMit4 and DXMit42) from a Fawn Hooded rat into a GK rat, wherein the rat does not comprise GK alleles at markers D3Rat57, D11Mgh5, D12Rat22, D1Rat 291, D1Mit18, D1Mit34, D1Mgh12, and D1Rat85, and wherein the rat is obtained by breeding the T2DN rat of claim 1 with a second rat."**

Claim 8 is rewritten as follows:

--**"A rat comprising mitochondrial genome at loci on chromosomes 2 (D2Rat12), 11 (D11Rat93), 16 (D16Rat15), 19 (D19Rat59), and X (DXMit4 and DXMit42) from a Fawn Hooded rat into a GK rat, wherein the rat does not comprise GK alleles at markers D3Rat57, D11Mgh5, D12Rat22, D1Rat 291, D1Mit18, D1Mit34, D1Mgh12, and D1Rat85, wherein the rat is obtained by breeding the rat of claim 4 with a second rat."**

Claim 11 is rewritten as follows:

--**"A method of evaluating the effect of a test compound on diabetes and diabetic nephropathy in a T2DN rat comprising the steps of:**

(a) exposing the test compound to a T2DN rat comprising mitochondrial genome at loci on chromosomes 2 (D2Rat12), 11 (D11Rat93), 16 (D16Rat15), 19 (D19Rat59), and X (DXMit4 and DXMit42) from a Fawn Hooded rat into a GK rat, wherein the rat does not comprise GK alleles at markers D3Rat57, D11Mgh5, D12Rat22, D1Rat 291, D1Mit18, D1Mit34, D1Mgh12, and D1Rat85, and wherein the T2DN rat would develop progressive proteinuria and glomerulosclerosis leading to diabetic nephropathy in the absence of the test compound, and

(b) comparing the development of diabetes and diabetic nephropathy in the treated T2DN rat with a control T2DN rat which has not been exposed to the test compound."

Claim 12 is rewritten as follows:

--**"A method of evaluating the effect of a test compound on diabetes and diabetic nephropathy in a T2DN rat comprising the steps of:**

(a) exposing the test compound to a genetically altered T2DN rat comprising mitochondrial genome at loci on chromosomes 2 (D2Rat12), 11 (D11Rat93), 16 (D16Rat15), 19 (D19Rat59), and X (DXMit4 and DXMit42) from a Fawn Hooded rat into a GK rat, wherein the rat does not comprise GK alleles at markers D3Rat57, D11Mgh5, D12Rat22, D1Rat 291, D1Mit18, D1Mit34, D1Mgh12, and D1Rat85 and wherein the T2DN rat would develop progressive proteinuria and glomerulosclerosis leading to diabetic nephropathy in the absence of the test compound, and

(b) comparing the development of diabetes and diabetic nephropathy in the treated genetically altered T2DN rat with a control genetically altered T2DN rat which has not been exposed to the test compound, wherein the treated and the control rats comprise the same genetic modification."

3. The following is the Examiner's statement for allowance:

The claimed invention is drawn to a specific rat diabetes model, wherein the rat develops symptoms of type II diabetes and progressive diabetic nephropathy with nodule formation, leading to end stage renal disease (i.e., closely resembling the human disease). It is noted that the art teaches non-insulin-dependent diabetic OLETF rats, wherein the OLETF rats have been identified as a good model for the human disease because they develop progressive nephropathy with nodule formation (see Nakamura et al., Diabetes, 1997, 46: 895-899, of record; Kawano et al., U.S. Patent No. 5,789,652). However, these rats are distinct from the claimed T2DN rats because they are derived from Long-Evans rats by mating male rats with abnormal glucose tolerance with females of the same litter (see Kawano et al.). The art also teaches several other rat diabetes models, but none of these is an adequate model for the human disease because they do not reproduce the human disease. Therefore, the prior art does not teach the claimed T2DN rat.

The claimed T2DN rat has utilities in understanding the pathogenesis of the human disease and in screening for possible therapeutic agents capable of ameliorating diabetic nephropathy.

Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633